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Asymptomatic Bacteriuria: Significance for Different Patient Population

Thomas Nelius, Stephanie Filleur and Jonathan S. Nelson
 Texas Tech University Health Sciences Center
 Departments of Urology and Microbiology
 Lubbock
 USA

1. Introduction

Infections of the urinary tract (UTI) are one of the most common infections for which antibiotics are prescribed. Asymptomatic bacteriuria, or asymptomatic urinary infection, is a common condition (Nicolle, 2003). *Based on the microbiological definition, urinary tract infections are characterized by the presence of $\geq 10^5$ colony-forming units per ml (CFUs/mL) of a single bacterial species or multiple organisms in two consecutive urine specimens, properly collected from a person with symptoms or signs of a UTI* (Rubin et al., 1992). However, the presence of a significant quantity of bacteria in the urine of an asymptomatic patient is known as asymptomatic bacteriuria. Quantitative criteria to establish the diagnosis of significant bacteriuria in an asymptomatic person are: 1. at least 10^5 CFUs/mL of urine in a voided midstream, so called clean-catch specimen; and 2. at least 100 CFUs per mL of urine obtained by bladder catheterization. Despite several decades of research, there is still a considerable amount of controversy about the adequate management of bacteriuria. A common dilemma in clinical medicine is whether or not to treat asymptomatic bacteriuria. It is now recognized that certain patient characteristics can lead to the development of symptomatic infections based on an asymptomatic bacteriuria. For several clinical scenarios, the antibiotic treatment of asymptomatic bacteriuria has been shown to improve patient outcomes. Based on clinical trials conducted over the last few decades, better recommendations for the management of bacteriuria in different patient population could be established. The Infectious Diseases Society of America (IDSA) established guidelines for the screening and treatment of asymptomatic bacteriuria (Nicolle et al., 2005). The optimal management depends significantly on specific patient characteristics, co-morbidities, and risk factors. Recent studies could prove that for certain patient populations, screening and treatment is beneficial or may be beneficial. However, for other clinical scenarios, screening and treatment for asymptomatic bacteriuria has not proven to be beneficial and therefore is highly controversial. Importantly, overtreatment of asymptomatic bacteriuria is a quality, safety, and cost issue. Recent studies have revealed a substantial gap between clinical practice, published guidelines, and recommendations (need reference). Treating physicians need to be aware that because of an increasing antimicrobial resistance, it is important to treat patients only if there is clear evidence of potential benefits. Therefore, in this chapter we review the most recent literature and provide up-to-date information for treating physicians on how to diagnose and when to treat asymptomatic bacteriuria.

1.1 Historical aspects

The use of quantitative urine cultures for the microbiological diagnosis of UTI was suggested and validated more than 50 years ago (Kass, 1957, 1962). If bacteria were isolated in quantitative counts of $\geq 10^5$ colony-forming units (CFU)/mL in a voided urine specimen from asymptomatic patients, the condition was described as asymptomatic bacteriuria. Interestingly, in this patient population the isolated organisms were always the same in paired specimens obtained by urinary catheterization. Quantitative counts of $\leq 10^5$ colony-forming units (CFU)/mL in a voided urine specimen usually resulted in a negative paired catheterized specimens. Therefore, $\leq 10^5$ colony-forming units (CFU)/mL in voided specimens were considered as contamination. The general acceptance and widespread use of this technique identified several clinically asymptomatic patient populations with an increased prevalence of positive urine cultures (Kunin, 1966). Specifically, pregnant women, patients with urogenital abnormalities, and patients with indwelling urethral catheters demonstrated a higher incidence of asymptomatic bacteriuria (Kunin, 1966). Antibiotic treatment of asymptomatic bacteriuria in pregnant women resulted in a significantly reduced incidence of pyelonephritis (Kass, 1962), which is considered an important concern in pregnancy. The obvious benefits of eradicating bacteriuria in asymptomatic pregnant women were interpreted to be generally applicable. Therefore, other patient populations with asymptomatic bacteriuria were also treated ordinarily (Kass, 1962). This treatment strategy was not based on clinical studies or facts, rather on the assumption that asymptomatic bacteriuria was consistently harmful in all populations and necessitated antibiotic treatment (Nicolle, 2006). Both basic and clinical research conducted over the last few decades, including long-term cohort studies and prospective randomized comparative trials in defined populations with asymptomatic bacteriuria, have improved the understanding of this clinical condition and addressed appropriate management (Nicolle, 2006).

2. Material and methods

To identify all relevant materials, comprehensive literature searches were performed via the data sources: MEDLINE, EMBASE, CINAHL and OVID using the key words: asymptomatic bacteriuria, pyuria, urinary tract infection, urine culture, UTI, antibiotic treatment. Relevant articles and references between 1962 and 2010 were reviewed and analyzed for data on the association between asymptomatic bacteriuria and antibiotic treatment. Reference lists from relevant review articles were also searched. Only articles published as formal papers in peer-reviewed journals were selected for inclusion if they reported outcomes of interest including potential benefits of antibiotic treatment for asymptomatic bacteriuria. The data base searches resulted in 1400 articles, of which 356 of 1400 pertained directly to asymptomatic bacteriuria and antibiotic treatment. The entirety of these articles was reviewed, forming the basis for the current review.

3. Results

3.1 Causes and pathogenesis of asymptomatic bacteriuria

The normal upper and lower urinary tract is considered sterile, except for the distal end of the urethra. Colonization with bacteria or development of an asymptomatic bacteriuria occurs due to ascension of bacteria into the urinary bladder or into the upper urinary tract,

including the kidneys. Typically, the bacteria isolated from patients with asymptomatic bacteriuria are part of the normal colonizing flora of the periurethral area, vagina, or bowel. The most common organism isolated from patients with asymptomatic bacteriuria is almost uniformly *Escherichia coli* (Bennett et al., 1995, Hooton et al., 2000, Kunin et al., 1964, Leblanc & McGanity, 1964, Nicolle et al., 1983, Nicolle et al., 1987, Zhanel et al., 1995), with only two exceptions. In elderly institutionalized men, common organisms include *Pseudomonas mirabilis*, *Providencia* spp, and *Pseudomonas aeruginosa*. In patients with spinal cord injuries, only *Klebsiella pneumonia* and *Streptococcus* spp are more common (Bennett et al., 1995, Nicolle et al., 1983). However, a large variety of different bacteria can be isolated, including *Citrobacter* spp, *Enterococcus* spp, coagulase-negative staphylococcus species, and others (Bennett et al., 1995, Hooton et al., 2000, Kunin et al., 1964, Nicolle et al., 1983, Nicolle et al., 1987, Zhanel et al., 1995). The mechanisms causing asymptomatic bacteriuria are still not fully understood. Characterization and comparison of *Escherichia coli* strains from patients with asymptomatic bacteriuria and acute uncomplicated urinary infection/acute nonobstructive pyelonephritis revealed a lower frequency of genetic markers or phenotypic expression of potential virulence factors (Geerlings et al., 2001, Stenqvist et al., 1987, Svanborg & Godaly, 1997). The expression of virulence factors seems to be a key event determining symptoms or persistence (Andersson et al., 1991). Interestingly, several authors reported a local response even in the absence of clinical symptoms. A local response includes mainly pyuria (Bachman et al., 1993, Hooton et al., 2000, Kincaid-Smith & Bullen, 1965, Kunin et al., 1964, Nicolle, 1997, 2001, Zhanel et al., 1995), although other local inflammatory or immune markers, including cytokines and urinary immunoglobulins, may also be present (Nicolle, 1997, Svanborg & Godaly, 1997).

3.2 Diagnostic

3.2.1 Urine culture

To establish the diagnosis of bacteriuria, a urine specimen for culture is necessary. There is a general agreement for men and women in the definition of the diagnostic approach in order to make the diagnosis bacteriuria (Evans et al., 1978, Gleckman et al., 1979, Hooton et al., 2000, Kunin, 1966, Lipsky et al., 1987, Ouslander et al., 1987, Rubin et al., 1992).

For men, a quantitative count of a potential uropathogen of $\geq 10^5$ CFU/mL in a single voided midstream clean-catch specimen or at least 100 CFUs per mL of urine from a catheterized specimen are reliable for identification of bacteriuria (Gleckman et al., 1979, Lipsky, 1989, Lipsky et al., 1987, Saint & Chenoweth, 2003, Warren et al., 1982). Exception exists for elderly men with external condom catheters. For this patient population, a quantitative count of $\geq 10^5$ CFU/mL is necessary for the diagnosis. The results were obtained by comparison with bacterial counts of concurrent catheterized specimens (Nicolle et al., 1988, Ouslander et al., 1987). Quantitative counts $\leq 10^5$ CFU/mL are consistent of bacterial colonization with periurethral organisms or contamination from the condom catheter itself.

For women, a quantitative count of a potential uropathogen of $\geq 10^5$ CFU/mL in at least two consecutive voided midstream clean-catch specimen or at least 100 CFUs per mL of urine from a catheterized specimen are reliable for identification of bacteriuria and the recommended standard (Kunin, 1966, Nicolle, 2003, Nicolle et al., 2005, Rubin et al., 1992). Identification of bacteriuria in women based on a single voided specimen has been reported to be 80% specific, and 95% specific for two specimens (Kunin et al., 1964, Rubin et al., 1992). The fact that there is an 80% concordance rate between the first and the second voided urine

specimen is often related to a transient bacteriuria, a condition common in young women (Hooton et al., 2000).

According to the IDSA guideline, the criteria for identification of bacteriuria in specimens obtained from catheterized patients are similar for women and men. (Saint & Chenoweth, 2003). However, some authors defined bacteriuria differently in their studies, ranging from identification in a single voided urine (Geerlings et al., 2000, Hooton et al., 2000) to those requiring persistent bacteriuria from two or more specimens (Evans et al., 1978).

3.2.2 Nonculture urine tests

Nonculture urine tests are widely used in primary care settings to evaluate urinary symptoms or as a screening test. The sensitivity and specificity of nonculture urine tests are insufficient to diagnose bacteriuria in asymptomatic patients. Nonculture urine tests are the so called dipstick tests and are designed to identify leukocyte esterase and nitrite in the urine specimen. A urine dipstick leukocyte esterase test showing pyuria has a sensitivity of 75 to 96 percent and specificity of 94 to 98 percent (Sobel, 2005). However, the test is not specific enough and may also be positive with other inflammatory conditions of the genitourinary tract (e.g., vaginitis). Frequently, patient with asymptomatic bacteriuria do not have pyuria. The urine dipstick nitrite test has several limitations, and therefore has a high false-negative rate. Importantly, the test is unable to diagnose bacteriuria with non-nitrite-producing pathogens (Kunin & DeGroot, 1975). Both a delay between urine sample collection and testing, and insufficient time since the last void for bacteria to produce sufficient amount of nitrites to appear at detectable levels contribute to the high false-negative rate (Goossens et al., 1985, Kunin & DeGroot, 1975, McNair et al., 2000). A higher specificity can be achieved by combining the leukocyte esterase and nitrite tests results, but the quantitative urine culture remains the optimal screening test. A microscopic urine analysis is a useful additional test for the identification of bacteriuria (Colgan et al., 2006).

3.3 Epidemiology

Although asymptomatic bacteriuria is a common condition, its prevalence differs significantly between certain patient population. The prevalence depends on age, sex, sexual activity, pregnancy, the presence of genitourinary abnormalities, indwelling urinary catheters, and co-morbidities including diabetes mellitus and immunosuppressive conditions (Bakke & Digranes, 1991, Chaudhry et al., 1993, Nicolle, 1997, 2003, Waites et al., 1993, Zhanel et al., 1991). It more often affects women than men (Colgan et al., 2006). Studies could show that the type of organisms isolated from patients with asymptomatic bacteriuria is influenced by certain patient characteristics: e.g. a healthy person will most likely harbor *E. coli*, while a nursing home resident with a catheter is more likely to have a multi-drug-resistant polymicrobial flora (e.g., *P. aeruginosa*). Enterococcus species and gram-negative bacilli are common in men. In order to describe the prevalence for certain subgroups, a modified classification from Nicolle was used (Nicolle, 2003).

3.4 Prevalence and treatment outcomes for certain patient population

3.4.1 Healthy, young populations

Pediatric Population

The prevalence of asymptomatic bacteriuria in full-term infants and in premature infants is less than 1% and 3%, respectively (Edelmann et al., 1973). If bacteriuria is present in

neonates and infants, congenital malformations, especially vesicoureteral reflux, need to be rule out (Whitworth, 1981). Even an asymptomatic bacteriuria can cause renal scars and subsequently renal insufficiency and hypertension later in life. Antibiotic therapy maybe recommended under these circumstances. In preschool aged children, the prevalence is approximately 0.8% for girls and is insignificant for boys, and is almost never identified beyond the newborn period (Siegel et al., 1980). Its prevalence subsequently increases slightly with age (Siegel et al., 1980). In school-age girls, the prevalence is around 2%-5% (Kunin, 1985). Two randomized controlled trials did not report significant differences in outcome when treating asymptomatic bacteriuria in girls with antibiotics or not (Lindberg, 1975, Savage et al., 1975). Others could show that girls with asymptomatic bacteriuria do experience more frequent symptomatic urinary infection compared with those without bacteriuria (Emans et al., 1979, Gillenwater et al., 1979). Antibiotic treatment in this clinical setting showed only little benefit (Sequelae of covert bacteriuria in schoolgirls. A four-year follow-up study, 1978, Covert bacteriuria in schoolgirls in Newcastle upon Tyne: a 5-year follow-up. Newcastle Covert Bacteriuria Research Group, 1981, Gillenwater et al., 1979, Lindberg et al., 1978, Siegel et al., 1980, Welch et al., 1976, Wettergren et al., 1990). Noteworthy, spontaneous resolutions are common, as well recontaminations and persistence for many years (Hansson et al., 1989, Kunin, 1985). More importantly, initiated antibiotic treatment in these conditions resulted subsequently in a higher incidence of symptomatic urinary infection in the *post-treatment* period (Hansson et al., 1989). Therefore, screening for or treatment of asymptomatic bacteriuria in healthy children is not recommended (Kemper & Avner, 1992, Lindberg et al., 1978, Wettergren et al., 1990).

Non-pregnant premenopausal, women

The prevalence of asymptomatic bacteriuria in young, healthy, premenopausal, non-pregnant women was reported between 0.7% and 5.2% (Bengtsson et al., 1998, Kunin & McCormack, 1968). It increases with age and sexual activity (Kunin & McCormack, 1968). Even without urological abnormalities, it is a common finding and shows a correlation with the use of a diaphragm or spermicide for birth control (Hooton et al., 2000, Peddie et al., 1986). A number of studies demonstrate that approximately 30% of women with asymptomatic bacteriuria will develop symptomatic episodes within 1 year (Asscher et al., 1969, Gaymans et al., 1976), however none of the studies show any benefit from treating (Alwall, 1978, Freedman, 1975, Gleckman, 1976, Tencer, 1988). In this patient population asymptomatic bacteriuria is not associated with any long-term adverse outcomes. Noteworthy, antimicrobial therapy given in this setting is rather associated with an increased frequency of symptomatic infection in the immediate *post-antibiotic* period (Foxman et al., 2001, Smith et al., 1997). Therefore, screening for and treatment of asymptomatic bacteriuria are not recommended for healthy, premenopausal, non-pregnant women. Moreover, eradication of bacteriuria by antibiotic courses is difficult, time consuming, costly, and potentially hazardous (Raz, 2003).

Pregnant women

The prevalence of asymptomatic bacteriuria during pregnancy ranges between 2% to 7% and is similar to non-pregnant women of the same age (Little, 1966, Plache et al., 1981). Physiological changes during pregnancy, including dilatation of the ureters and renal pelvis, allow bacteria in the bladder to reach the kidneys and produce pyelonephritis (Shortliffe, 1986). 20% to 30% of bacteriuric pregnant women develop an acute pyelonephritis during

pregnancy if untreated, in contrast to only 1-3% of pregnant women who received antibiotics (Golan et al., 1989, Kasviki-Charvati et al., 1982). It is well documented that acute pyelonephritis in late pregnancy is associated with prematurity (Gilstrap et al., 1981, McGrady et al., 1985, Mittendorf et al., 1992). Asymptomatic bacteriuria in pregnancy has also been associated with low-birth-weight infants and the possibility of perinatal death (Platt, 1987, Romero et al., 1989, Schieve et al., 1994, Wadland & Plante, 1989). Treatment of bacteriuria in pregnancy resulted in a 90% risk reduction, and also decreases premature delivery (see Table 4) (Gratacos et al., 1994). Therefore, screening for and antibiotic treatment of asymptomatic bacteriuria in pregnant women are beneficial (Nicolle, 2003).

Healthy young men

Only limited data are reported on the association between asymptomatic bacteriuria and young men. According to the literature, it is uncommon in healthy young adult men (Lipsky, 1989). The reported prevalence ranges between 0% and 1.5% (Freedman, 1975, Wilson et al., 1986). No significant differences were reported for heterosexual and homosexual men (Wilson et al., 1986). One clinical study reporting 1.5% prevalence of asymptomatic bacteriuria in young men could show that after careful questioning, all bacteriuric men had lower urinary tract symptoms, including dysuria (Wilson et al., 1986). Taking into consideration the limited reported results, asymptomatic bacteriuria is not a relevant clinical issue in young healthy men, and therefore, screening for asymptomatic bacteriuria is not recommended.

3.4.2 Elderly populations

Community and institutionalized residents

The prevalence of asymptomatic bacteriuria in the elderly populations is common and differs significantly between community residents and residents in long-term care facilities (Nicolle, 1997, 2003, 2006). The prevalence ranges between 6% to 50% in women, and 6% to 34% in men for community residents and increases with age (Boscia et al., 1986, Kunin & McCormack, 1968). An even higher prevalence was reported for elderly institutionalized residents (25% to 50% in women, and 15% to 40% in men) (Nicolle, 1997, 2003, 2006). Decreased estrogen effect on the genitourinary mucosa, urinary incontinence, prior urologic events including genitourinary surgery, urologic abnormalities such as cystoceles, as well as recurrent symptomatic infection in elderly women contribute to asymptomatic bacteriuria (Raz et al., 2000). For men, prostatic hypertrophy with bladder outlet obstruction was reported to be the major predisposing factor for the development of asymptomatic bacteriuria. Also the use of an external condom catheter to manage incontinence in men increases its prevalence (Ouslander et al., 1987). Several studies, including prospective, randomized studies, did not find any benefits when treating asymptomatic bacteriuria in this patient population. Specifically, no decrease in symptomatic episodes (Boscia et al., 1987, Nicolle et al., 1983, Nicolle et al., 1987) and no differences in morbidity and mortality were seen (Abrutyn et al., 1994, Nicolle et al., 1983, Nicolle et al., 1987, Ouslander et al., 1995). Noteworthy, residents treated for asymptomatic bacteriuria were reported to have an increased reinfection rate with resistant organisms and side effects from antibiotic treatment (Nicolle et al., 1987). Therefore, screening for or treatment of asymptomatic bacteriuria in elderly residents in the community and or institutionalized residents is not recommended (Nicolle, 2001, Pels et al., 1989).

3.4.3 Patients with chronic medical conditions

Diabetes mellitus

Several studies reported a prevalence of bacteriuria in diabetic women of 7% to 13% (Brauner et al., 1993, Geerlings et al., 2000, Zhanel et al., 1995), which is approximately a 3-fold higher prevalence than in non-diabetic women (Zhanel et al., 1991). Diabetic men do not show higher prevalence rates than non-diabetics (Zhanel et al., 1990, Zhanel et al., 1991). The reasons for the high prevalence in women are still not well understood. A main factor for asymptomatic bacteriuria might be the development of an autonomic neuropathy leading to impaired bladder voiding (Patterson & Andriole, 1997). The duration of diabetes mellitus and the presence of long-term diabetic complications such as nephropathy, retinopathy, peripheral vascular disease, and neuropathy were reported to be associated with asymptomatic bacteriuria (Vejlsgaard, 1966, Zhanel et al., 1995). There is evidence, that symptomatic urinary infection may be potentially more severe in diabetic than non-diabetic patients (Patterson & Andriole, 1997). Both, the severity of symptomatic infection and the higher prevalence of bacteriuria in diabetic women has led to the assumption that treatment of asymptomatic bacteriuria in this patient population might be beneficial (Screening for asymptomatic bacteriuria, hematuria and proteinuria. The U.S. Preventive Services Task Force, 1990). Several studies, including long term and/or prospective do not suggest that asymptomatic bacteriuria is harmful in diabetic women (Geerlings et al., 2001, Semetkowska-Jurkiewicz et al., 1995). Moreover, treatment did not show any significant benefits in terms of improved glucose control or delayed development of long-term complications of diabetes mellitus (Geerlings et al., 2001, Semetkowska-Jurkiewicz et al., 1995). Antimicrobial treatment of bacteriuria did not decrease the frequency or severity of symptomatic urinary infection. However, greater antimicrobial exposure and a higher frequency of adverse drug effects with antimicrobial therapy and a high rate of recurrent asymptomatic bacteriuria were observed following therapy (Harding et al., 2002). In summary, screening for and treatment of asymptomatic bacteriuria in diabetic women with asymptomatic bacteriuria and normal renal tracts should not be recommended.

Patients with spinal cord-injuries

The neurologic bladder dysfunction is the key event in the development of asymptomatic bacteriuria in this patient population (Erickson et al., 1982, Sanderson & Weissler, 1990, Schlager et al., 1995, Sotolongo & Koleilat, 1990). The prevalence of asymptomatic bacteriuria remains high independently of the method of bladder emptying (see Table 6-need ref). The preservation of a low pressure urinary tract decreased morbidity and mortality secondary to urosepsis and renal failure dramatically in this patient population (Hackler et al., 1989). However, symptomatic urinary tract infections are still a significant issue (DeVivo et al., 1985, Ditunno & Formal, 1994). Clinical studies, including prospective cohort studies and placebo-controlled trials show no decrease in symptomatic infection with antibiotic therapy for asymptomatic bacteriuria (Mohler et al., 1987) and no progression to renal failure with asymptomatic bacteriuria were observed, as long as a low urinary bladder pressure was maintained (Sotolongo & Koleilat, 1990). Therefore, screening for or treatment of asymptomatic bacteriuria in spinal cord injury populations is currently not recommended (Cardenas & Hooton, 1995, Ditunno & Formal, 1994).

Kidney transplant patients

Asymptomatic bacteriuria is a very common event after kidney transplantation, especially during the immediate post-transplantation period. Often the differentiation between

asymptomatic bacteriuria and infection is difficult because of the presence of immunosuppressive medications, which can suppress symptoms and signs of infections. Ramsey et al. diagnosed 65 bladder infections in 35 of 65 transplant recipients during 14.7 months follow-up. In this study, 91% of the patients were asymptomatic and 57% of the infections occurred within 1 month, and approximately 80% by 6 months (Ramsey et al., 1979). In another study by Prat et al., 185 of 299 kidney transplant patients had at least one episode of infection with 96% of the episodes asymptomatic (Prat et al., 1985). Patients with persistent infection and urologic complications often experienced sepsis and graft loss. However, graft survival was not associated with the presence or absence of bacteriuria in patients without urologic complications (Griffin & Salaman, 1979, Ramsey et al., 1979). The frequency of both asymptomatic and symptomatic urinary infection in renal graft recipients has declined due to improved early post-transplantation management including routine perioperative antibiotics, short-term urethral catheterization, and use of long-term prophylactic antibiotics to prevent all post-transplant infections (Fox et al., 1990, Hoy et al., 1985). Fiorante et al. reported no differences in renal allograft prognosis between those who do not develop asymptomatic bacteriuria and those who do develop asymptomatic bacteriuria and are systematically treated. Systematic treatment of asymptomatic bacteriuria however, may reduce the incidence pyelonephritis (Fiorante et al.). Similar results were reported by others (Lyerova et al., 2001, Takai et al., 1998). Therefore, evidence to support screening recommendations in the post-transplant period is still deficient. According to the Immunocompromised Host Society Consensus Conference, periodic monitoring for urinary infection in post-transplant might be beneficial, but a specific frequency of screening or clear recommendations for therapy if bacteriuria is identified were not given (Snydman, 2001).

Other immunocompromised patients

Other than kidney transplantation, no convincing data has been reported so far on the relationship between asymptomatic bacteriuria and organ transplantation, including bone marrow transplantation. For this reason, post-transplant screening and treatment for asymptomatic bacteriuria is highly controversial for this patient population (Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients, 2000, Snydman, 2001). Chemotherapy-induced granulocytopenia during the treatment of a variety of malignancies possibly represents a risk factor for patients with asymptomatic bacteriuria to develop urinary tract infections (Gurwith et al., 1979). Another immunosuppressive condition with a higher prevalence of asymptomatic bacteriuria is the infection with HIV (Awolude et al., 2011). Several studies suggest a correlation between low CD4+ counts and the presence of asymptomatic bacteriuria (Awolude et al., 2011, De Pinho et al., 1994, Hoepelman et al., 1992). No articles were identified addressing the use of antibiotic treatment for this patient population. The reason for the higher prevalence of asymptomatic bacteriuria and low CD4 counts is not well understood. Based on the lack of data in this clinical setting, routine screening and treatment of patients with HIV and asymptomatic bacteriuria cannot be recommended.

3.4.4 Patients with urological or gynaecological devices

Catheterized patients

Clear differences were reported in the literature on the relationship of asymptomatic bacteriuria and short- and long-term transurethral bladder catheterization. No reports for

suprapubic tubes were found in the peer-reviewed literature. The prevalence of asymptomatic bacteriuria correlates with several influencing factors, including the type and duration of bladder catheterization, qualification of the health-care personnel and the catheter system and care (MacFarlane, 1984).

Patients with temporary transurethral or suprapubic indwelling catheters

Single bladder catheterization is associated with less than 1% risk of developing asymptomatic bacteriuria for patients in an ambulatory setting (Garibaldi et al., 1974). The development of asymptomatic bacteriuria even after placement of short-term transurethral catheters is significant. Short term is defined as less than 30 days of bladder catheterization. The prevalence of asymptomatic bacteriuria increases on a daily basis by 2%-7% (Tambyah & Maki, 2000). A prevalence of nearly 100% was reported for elderly patients with an indwelling transurethral catheter and an open urine collecting bag system (Uehling et al., 1985), and 20% for patients with a closed urine collection system (MacFarlane, 1984). Early clinical studies could not demonstrate any benefits when treating patients with short-term indwelling catheters with antibiotics and asymptomatic bacteriuria (Butler & Kunin, 1968). A common dilemma is that approximately 80% of all patients with transurethral catheters are treated with antibiotics for other reasons, therefore it is difficult to define the significance of asymptomatic bacteriuria for this patient population (Johnson et al., 1990, Riley et al., 1995). It is noteworthy that the development of asymptomatic bacteriuria in patients with a permanent catheter is practically inevitable. According to Nicolle (Nicolle, 2003) screening and treatment of bacteriuria for patients with short-term indwelling catheters is recommended only for patients with certain risk factors, such as a pregnant woman or those undergoing an invasive urologic procedure.

Patients with permanent transurethral or suprapubic indwelling catheters

Long term or chronic indwelling catheters are defined as more than 30 days of bladder catheterization. For this patient population bacteriuria is universal. The main reason for the development of bacteriuria under these circumstances is the presence of a biofilm, a material composed of bacteria and extracellular bacterial substances in combination with certain urinary components including Tamm-Horsfall protein, magnesium, and calcium (Donlan & Costerton, 2002). Several studies suggest that patients with a chronic indwelling catheter have a higher morbidity from symptomatic urinary infection compared to patients without a catheter (Orr et al., 1996, Warren et al., 1987). Therefore, several prospective randomized studies were conducted to define the role of antibiotic treatment for this clinical scenario. Antibiotic treatment did not reduce the frequency of fever in treated patients compared to untreated patients with asymptomatic bacteriuria. A higher percentage of resistant organisms were encountered in the treatment group after antibiotic treatment and that antibiotic treatment rarely eliminated the bacteriuria (Alling et al., 1975, Warren et al., 1982). Therefore, patients with long-term indwelling catheters should not be screened and treated with antibiotic therapy for asymptomatic bacteriuria. None of the published studies could demonstrate any benefits of antibiotic treatment, but did demonstrate potential harm for the patient. However, antibiotic treatment might be considered for patients at high risk for certain complications, for instance infection of prosthetic devices (Raz, 2003).

Other indwelling devices

The mainstay in the treatment of ureteral obstruction is the use of ureteral stents. Similar to transurethral *catheters*, these devices are subject to biofilm development and asymptomatic

bacteriuria (Riedl et al., 1999). Often it is difficult to differentiate between asymptomatic bacteriuria and bladder infection, as patients frequently report dysuria, frequency and urgency as a reaction to the indwelling ureteral stent. Studies have shown that prophylactic antibiotic treatment did not reduce bacterial colonization or prevent stent obstruction (Riedl et al., 1999). The evidence for screening and treatment in this setting is sparse and therefore not recommended. Fallahian et al. describe the use of intrauterine devices as a risk factor for urinary tract infections. For patients with asymptomatic bacteriuria, an intrauterine device therefore might not be the method of choice, and other contraceptive methods should be preferred (Fallahian et al., 2005).

3.4.5 Patients undergoing surgical intervention

Urological surgery

Patients with asymptomatic bacteriuria undergoing any surgical procedures or manipulations of the genitourinary tract are nearly uniformly at risk to develop complications. Surgery or trauma causes mucosal injuries allowing bacteria to penetrate the tissue causing local infection, or to invade the blood circulation resulting in bacteremia and/or sepsis. If left untreated, asymptomatic bacteriuria prior to the surgery resulted in bacteremia in 25%-80% of the patients (Olson & Cookson, 2000). Other authors could demonstrate that antibiotic treatment prior to the surgery can prevent bacteremia and sepsis (Grabe, 2001, Olson & Cookson, 2000). Olson et al. recommend antibiotic treatment only immediately before the procedure, since earlier initiation can result in reinfection with resistant bacterial strains (Olson & Cookson, 2000). Grabe suggests treatment of asymptomatic bacteriuria before urodynamic studies, ureteral stent placements, ureteroscopic procedures and transurethral resection of the prostate (Grabe, 2001). However, no general consensus exists for which urologic intervention requires preoperative treatment of asymptomatic bacteriuria (Grabe, 2001).

Ileal Conduit and Orthotopic Neobladder

The treatment of asymptomatic bacteriuria in patients with ileal conduit and orthotopic neobladder is controversial (Zhanel et al., 1990). Guinan et al. described the bacterial milieu in patients with ileal conduit (Guinan et al., 1972). The terminal ileum is in nearly 100% of the patients sterile. After creation of an ileal conduit the mucosa is rapidly colonized. The most common organisms are *Proteus*, *Pseudomonas* and *E. coli*. Aggressive treatment is recommended for patients with pyelonephritis or systemic signs of illness (Guinan et al., 1972).

Other surgical interventions

A small number of studies have evaluated the risk of deep joint infection after joint replacement surgery associated with the preoperative presence of asymptomatic bacteriuria. A retrospective analysis of 277 patients undergoing 364 total joint replacements showed that 35 patients had evidence of preoperative or perioperative asymptomatic bacteriuria. Joint infections were observed in 3 patients (1.1%) 9, 19, and 45 months. None of the joint infections were related to perioperative asymptomatic bacteriuria (Ritter & Fechtman, 1987). Glynn and Sheehan reported in a retrospective analysis that 55 of 299 patients admitted for hip or knee arthroplasty had asymptomatic bacteriuria and 2 patients were symptomatic upon admission (Glynn & Sheehan, 1984). Routine perioperative antibiotic treatment initiated pre or postoperatively was sufficient to prevent infection of the implant. Deep joint

infection was not seen in any patients at 3-month follow-up, prompting the authors to conclude that asymptomatic bacteriuria is common and should not be a cause for postponement of surgery and that treatment with antibiotics can be implemented at any time perioperatively. In conclusion, asymptomatic bacteriuria may be a reservoir for bacterial contamination of the wound, or may identify a patient at increased risk of infection at any site, including implants, without having a causal relationship (Nelson et al., 1983). Present guidelines recommend to identify and treat any infection remote to the surgical site before an elective operation. It is only an assumption that this recommendation also includes asymptomatic bacteriuria (Mangram et al., 1999). However, screening and treatment of asymptomatic bacteriuria before any surgical procedures other certain urological procedures is currently not recommended. Coincidentally, the perioperative antibiotic prophylaxis given for most procedures is sufficient to suppress or eradicate asymptomatic bacteriuria and prevent symptomatic infections in the vast majority of cases.

4. Discussion

Asymptomatic bacteriuria is a common clinical finding in several different patient populations. A higher prevalence exists in patients with morphological or functional defects of the genitourinary tract and with indwelling urological devices. However, healthy individuals may also have asymptomatic bacteriuria. The central question for physicians and health care professionals is whether or not to treat asymptomatic bacteriuria. Continuous improvement has been made over the last few decades in documenting the epidemiology of asymptomatic bacteriuria. Patient populations with a high prevalence are well described. However, the natural history and guidelines for management are still controversial. Sufficient evidence exists to recommend screening and treatment for some patient populations with a high prevalence of asymptomatic bacteriuria, while for other populations no such recommendations exist.

| Screening and treatment proven to be beneficial |
|--|
| Pregnancy |
| Prior to traumatic genitourinary procedures |
| Screening and treatment may beneficial |
| Renal transplant recipient, first 6 months post-transplant |
| Immunocompromised patients (e.g. malignancy-chemotherapy) |
| Infected kidney stones |
| Vesicoureteral reflux in young children |
| Women with persistent catheter-acquired bacteriuria after catheter removal |

Table 1. Potential benefits of screening and treatment for asymptomatic bacteriuria.

This dilemma is based on the lack of good evidence from clinical trials investigating direct management strategies. Antibiotic treatment is only recommended if it has been shown to improve patient outcome. Sufficient evidence exists to screen and treat asymptomatic bacteriuria in pregnant women and patients undergoing traumatic urological interventions (table 1). *Young children with vesicoureteral reflux, renal transplant recipients, transplant recipients during the first 6 months post-transplant, immunocompromised patients (e.g. malignancy-chemotherapy), and women with*

persistent catheter-acquired bacteriuria after catheter removal might benefit from screening and treatment. However, the evidence is not strong enough to recommend it (table 1).

Screening for asymptomatic bacteruria is highly controversial in the patient populations listed in table 2. Treating asymptomatic bacteriuria in these patient populations has not been found to improve outcomes. In fact, antibiotic treatment in these patient populations may be associated with significant adverse effects. Possible side effects reported in the literature include the development of symptomatic infections, re-infection with organisms of increased antimicrobial resistance, and side effects directly related to the antibiotics (Nicolle, 2003). Overtreatment of asymptomatic bacteriuria is a substantial quality, safety, and cost issue.

| Screening and treatment controversial or not beneficial |
|--|
| Healthy infants |
| Healthy women or men |
| Elderly men and women in the community or in long-term care facilities |
| Women with diabetes |
| Patients with HIV infection |
| Patients with short-term and /or chronic-indwelling indwelling urethral catheters* |
| Patients using intermittent catheterization |
| Patients with neurologic impairment of bladder emptying |
| Patients with chronic urologic or gynecological devices |

* not recommended for patient care; may be appropriate to screen for bacteriuria for nosocomial infection surveillance or outbreak control.

Table 2. No proven benefits of screening and treatment for asymptomatic bacteriuria.

Therefore, it is crucial to treat patients with asymptomatic bacteriuria only if there is evidence of potential benefits. Urine cultures are commonly ordered as part of a routine work-up in hospitalized patients, despite lower urinary tract symptoms. More importantly, patients with asymptomatic bacteriuria are frequently treated under these circumstances, accounting for a substantial burden of inappropriate antibiotic use in hospitals (Silver et al., 2009). Similar findings have been reported for patients in long-term care facilities for the elderly (Walker et al., 2000). Many research questions, however, still remain to be addressed in future clinical trials. The potential benefits of treatment need to be weighed against no treatment in order to maximize patient safety.

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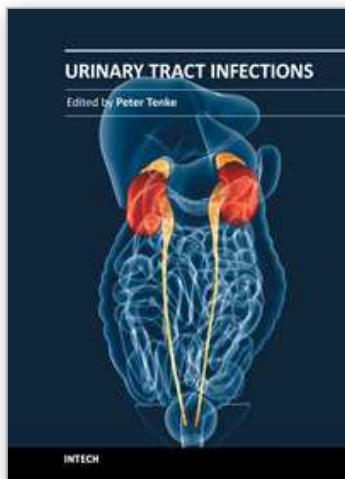
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Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, and they are also the leading cause of hospital-acquired infections. Therefore, the appropriate management of UTIs is a major medical and financial issue. This book covers different clinical manifestations of UTI, with special emphasis on some hard-to-treat diseases, and special conditions in respect of treatment; antibiotic resistance and the available alternative strategies for the prevention and treatment of UTIs and it deals with urinary tract infections in children. The aim of this book is to give a summary about the different aspects of the diagnosis, management and prevention of urinary tract infections for all medical disciplines.

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Slavka Krautzeka 83/A
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InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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